UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,354	06/30/2004	Masayo Higashiyama	2004_1016A	2612

513 7590 08/05/2008

WENDEROTH, LIND & PONACK, L.L.P.
2033 K STREET N. W.
SUITE 800
WASHINGTON, DC 20006-1021

EXAMINER	
RAE, CHARLESWORTH E	
ART UNIT	PAPER NUMBER
1611	
MAIL DATE	DELIVERY MODE
08/05/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,354	HIGASHIYAMA, MASAYO	
	Examiner	Art Unit	
	CHARLESWORTH RAE	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement is made of applicants' filing of the instant application as a Request for Continued Examination (RCE) under 37 CFR 1.1114.

Applicant's statement that support for the claim amendment may be found in the specification at page 8, lines 8-15, is acknowledged.

Status of the Claims

Claims 1-11 are currently pending in this application.

Claim 11 is withdrawn for examination purposes for being directed to non-elected subject matter.

Claim 1-10 are currently under examination.

Amendment

Claims 1 and 10 have been amended to specify that the metal chloride is a light-stabilizing agent.

Miscellaneous Comments

Applicant's request for a personal interview prior to this Office action is acknowledged. However, the examiner made several attempts to schedule an interview with applicant without any success. In view of the inability to schedule a timely interview, this Office action is being issued.

Claim rejections – 35 USC 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-10 are rejected under 103(a) as being unpatentable over Koida et al. (JP 2001261553A, abstract only; already made of record), in view of Kita et al (US Patent 6,307,052 B1;already made of record), and Remington's (Remington's Pharmaceutical Sciences. 1980; pages 1410-1419; already made of record).

It is noted that the light-stabilizing effect of the metal chloride salts encompassed by the instant claims is deem to be a characteristic that is inseparable from the chemical entity such that the light-stabilizing effect of said metal chloride salts is deemed to be coextensive with the claimed aqueous liquid preparation. Thus, the amendment of claims 1 and 10 to recite the light-stabilizing limitation does not confer patentability to the applicant's claimed invention.

Koida et al. teach bepotastine (i.e. (S)-4-[4-[(4-chlorophenyl)(2-pyridyl)methoxy]piperidino] butyric acid) has optical purity and has markedly improved

storage stability because of no occurrence of racemization (abstract). Claims 1, 4, 5, and 10 recite said compound.

Koida et al. do not teach applicant's instant claimed aqueous liquid preparation comprising bepotastine and a water-soluble metal chloride.

Kita et al. is added to show the general state of the art regarding aqueous preparations comprising benzenesulfonate and a compound containing a 2-pyridyl moiety having antihistaminic activity. Kita et al. teach that the benzenesulfonate and benzoate of (S)-4-[4-[(4-chlorophenyl)(2-pyridyl)methoxy]piperidino]butanoic acid possesses excellent antihistaminic and antiallergic agent activity (column 1, line 10 to column 3, line 19). Kita et al. teach that the acid addition salt has little hydroscopicity and excellent physiochemical stability so that it is a particularly suitable compound as a medicine for allergic skin diseases, allergic rhinitis, sneeze, mucus, cough due to respiratory inflammation such as a cold, and bronchial asthma (column 1, lines11-54).

Remington's Pharmaceutical Sciences (1980) is added to show the general state of the art regarding the utilization of metal chlorides in aqueous pharmaceutical preparations such as eye and nasal drops. Remington's teaches sodium chloride equivalents of certain medicinals in **aqueous** solution (pages 1411, column 2, to 1419; Appendix A; page 1419, Appendix B), which includes **calcium chloride** (page 1413), **potassium chloride** (page 1417), **sodium chloride** (page 1418), **benzalkonium chloride** (page 1413). Remington's teaches that besides water, certain other solvents are frequently employed in **nose drops**, ear drops, and other preparations to be used in various parts of the body (page 1410, column 2, second paragraph from the bottom).

The instant claim limitations regarding the concentration of the metal chloride as recited in claims 2, 4, and 10 (e.g. metal chloride concentration of 0.15-1.5 w/v%; acid addition salt concentration of 0.1-2 w/v%; pH 4-8.5; (S)-4-[4-[(4-chlorophenyl)(2-pyridyl)methoxy]piperidino] butyric acid monobenzenesulfonate and sodium chloride at not less than 0.2 w/v% and not more than 0.8 w/v%) are reasonably construed to be within the scope and skill of an artisan skilled in the art as these limitations represent optimization in preparing a stable composition (pages 1411, column 2, to 1419; Appendix A; page 1419, Appendix B). The pH range limitation of pH 4-8.5 as recited in claim 7 is encompasses the pH range routinely considered to be the optimum pH for aqueous preparations that are intended for use as eye drops.

It would have been obvious to one of ordinary skill at the time the invention was made to formulate the instant compound in an aqueous solution comprising a metal chloride. One would have been motivated to do so since Koida teaches similar compounds have antihistaminc activity and one would have reasonably assumed that the instant compounds also have this acitivity. Further, one would have been motivated to formulate the compounds in an aqueous solution since it is generally known in the art to formulate anti-histaminc agent into nasal and eye drops to relieve allergies and Remington teaches that it is convention to formulation eye drops and nasal drops with metal chlorides.

Thus, a person of ordinary skill in the art at the time the instant invention was made would have deemed it obvious to create the instant claimed invention with a reasonable predictability.

Relevant Art of Record

The below art reference made of record and relied upon is considered pertinent to applicant's invention.

Onuki et al. (US Patent Application Pub. No. 2004/0147605;already made of record) teach formulations comprising one or more antihistamine compound, including bepotastine besilate (page 2, para 0017, line 11).

Himmelstein et al. (US Patent 5,599,534; already made of record) teach pH-responsive reversible gelling compositions and liquid formulations for sustained delivery of therapeutic or diagnostic agents suitable for use as drop or spray instillable or topical drug delivery vehicles for drugs various drugs, including antihistamines and decongestants (e.g. pyrilmaine, chlorpheniramine, tetrahydrazoline, antazonline), which are particularly suitable for delivering pharmaceutical compounds to the ocular environment due to clarity and lubricating properties of the gel (col. 5, lines 32-49 and col. 8, line 51 to col. 9, line 9); flowable liquid forms of the composition are particularly useful for pharmaceutical formulations to be applied by drops (e.g. eye drops) or sprays (e.g. nasal sprays). See col. 7, lines 49-59; and col. 8, lines 29-34. Himmelstein et al. teach that the pH preferably is within the physiological range between pH 2.5 and 7.5 (col. 6, lines 35-39).

Kabra (US Patent 6,331,540) teach a method of enhancing the stability of an aqueous pharmaceutical composition containing fluoroquinolone and xantham gum and the step of adding to the composition a water-soluble calcium salt in an amount of at least 0.15 % (w/w), such that the composition is homogenous and has a turbidity rating

(NTU) < = 40 at room temperature (see cols. 5-6, including Table 3 and reference claim 1).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http:pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

16 July 2008
/C. R./
Examiner, Art Unit 1611

/Sharmila Gollamudi Landau/

Supervisory Patent Examiner, Art Unit 1611